

PCT

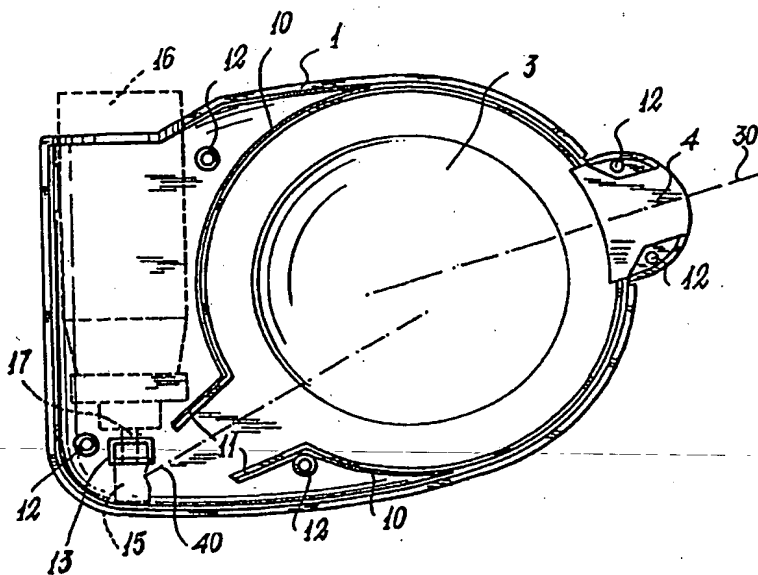
WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>A61M 15/00</b>	<b>A1</b>	(11) International Publication Number: <b>WO 99/12596</b> (43) International Publication Date: <b>18 March 1999 (18.03.99)</b>
(21) International Application Number: <b>PCT/EP98/05592</b> (22) International Filing Date: <b>3 September 1998 (03.09.98)</b> (30) Priority Data: <b>MU 7702049-9 5 September 1997 (05.09.97) BR</b> (71) Applicant (for all designated States except US): <b>CHIESI FARMACEUTICI S.P.A. [IT/IT]; Via Palermo, 26/A, I-43100 Parma (IT).</b> (72) Inventors; and (75) Inventors/Applicants (for US only): <b>CHIESI, Paolo [IT/IT]; Via Palermo, 26/A, I-43100 Parma (IT). DEL CORNO, Marco [IT/IT]; Via Romilli, 29, I-20139 Milano (IT). PANZA, Isabella [IT/IT]; Via Palermo, 26/A, I-43100 Parma (IT). VENTURA, Paolo [IT/IT]; Via Palermo, 26/A, I-43100 Parma (IT).</b> (74) Agent: <b>MINOJA, Fabrizio; Bianchetti Bracco Minoja S.r.l.; Via Rossini, 8, I-20122 Milano (IT).</b>		(81) Designated States: <b>AL (Utility model), AM (Utility model), AT, AT (Utility model), AU (Petty patent), AZ, BA, BB, BG (Utility model), BR, BY, CA, CH, CN (Utility model), CU, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), EE, EE (Utility model), ES, FI, FI (Utility model), GB, GE, GH, GM, HR, HU (Utility model), ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX (Utility model), NO, NZ, PL (Utility model), PT, RO, RU (Utility model), SD, SE, SG, SI, SK, SK (Utility model), SL, TJ, TM, TR (Utility model), TT, UA (Utility model), UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</b>  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>

(54) Title: **NOZZLE FOR USE IN MOUTH-INHALING FOR AEROSOL MEDICAMENTS**



(57) Abstract

An aerosol nozzle, comprising a socket provided with a seat to house a hollow stem of an aerosol dispensing pressurized can, said nozzle being shaped as a T, consisting of an upper bar and of a vertical stem, characterized in that the hole of said nozzle through which the aerosol dose is discharged is inclined with respect to the plane normal to the axis of said vertical stem.

*FOR THE PURPOSES OF INFORMATION ONLY*

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakhstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

NOZZLE FOR USE IN MOUTH-INHALING FOR AEROSOL MEDICAMENTS

The present invention relates to an aerosol nozzle, comprising a socket provided with a seat to house a hollow stem of an aerosol dispensing pressurized can.

Inhalation is the preferred system for delivering  
5 medicament particles into the lungs.

For this purpose pressurized cans containing the medicament and a propellant are used, the cans being provided with a metering valve which when manually operated dispenses metered doses of propellant-medicament  
10 mixture which atomizes through a nozzle as a finely powdered spray into the mouth of a patient.

It is generally known that only about 10% of the aerosol dose discharged by a pressurized can is capable to reach the lungs.

15 A similar percentage is expired or is deposited outside the oral cavity, whereas because of the impact of the high speed particles about 80% is deposited within the oropharyngeal cavity, swallowed systemically adsorbed and  
20 hence practically lost.

If the pressurized can is not used properly the quantity of medicament which reaches the site of action at the pulmonary level is further reduced and the therapeutic response is compromised.

25 Excessive aerosol depositing in the oropharyngeal cavity can also lead to undesirable effects either at systemic level as a consequence of the drug absorption, or at the local level, as in the case of corticosteroids, which can result in oral candidiasis.

30 The reasons for poor pulmonary penetration are known.

- 2 -

Even if a dispensing can for aerosol medicaments is used correctly, the availability of an inhaled medicament to the lungs depends largely on the size of the aerosol droplets.

5       The only particles that can penetrate into the lungs is any significant degree are those whose diameter is 1-5 thousandths of a millimetre (microns). An inhalation aerosol spray only contains a small amount of such particles as most of the medicament is bound to  
10 considerably larger droplets formed by a non-volatile propellant.

Thus, it is obvious that by reducing the droplet size of a spray it is also possible to reduce the particle size and hence to improve the pulmonary penetration of a  
15 medicament and the size of droplets is reduced as the volatilization of a propellant proceeds.

In an attempt to overcome the problems connected with the use of aerosol medicament, auxiliary delivery systems have been developed over the last decade for application  
20 to the nozzles of pressurized dispensing cans.

In the european patent EP-B-0475257 a mouth-inhaling device for use with pressurized cans for dispensing metered doses of medicament is described.

Said device is designed to favour the inhaling of a  
25 greater number of active particles and to avoid spraying the aerosol directly onto the mucosa of the oropharynx in order to safeguard the user against side effects deriving from direct spray into the mouth.

In this respect, the device has an expansion chamber  
30 shaped to create, by virtue of the speed at which the aerosolized material is expelled by the dispenser, a

- 3 -

vortex flow in which the particles remain in suspension for sufficient time to enable them to discharge their kinetic energy and allow substantial evaporation of the propellant, with a consequent reduction in the size and in the velocity of the particles, leading to a more efficient intrapulmonary delivery, while large size particles are centrifuged onto the walls of the chamber, to deposit on them.

The device comprises a body with a seat for housing a can provided with a stem for operating the can dispensing valve, a chamber for the collection and expansion of the aerosol dispensed by a discharge nozzle on the can, and a mouthpiece communicating with said chamber and projecting outwards from said body. The body has a substantially flat shape and the chamber is delimited by a curved wall, into a first peripheral portion of which there opens the inner end of the mouthpiece, and in a second peripheral portions of which, opposite the first, there is an aperture from which two walls extend outwards from the chamber to converge towards the can discharge nozzle and define a duct, the central plane of which is inclined to the central plane of said mouthpiece.

The aerosol dispensed by the can, when operated, penetrates into the expansion chamber and expands to circulate with a vortex flow which causes the solvent to evaporate and the flow movement to continue for a relatively long time, hence enabling only very small particles of the medicament to be drawn into the bronchial tree.

The structure and characteristics of the inhaler device are illustrated in Figure 1 to 4 in which:

- 4 -

Figure 1 is a perspective view of the inhaler device;

Figure 2 shows one of the two shells forming the device, viewed in the direction indicated by the lines 2-2 of Figure 1; and

5        Figure 3 and 4 are sections through the inhaler device on the lines 3-3 and 4-4 of Figure 1.

It can be seen from Figure 2 that in a peripheral portion of the curved wall 10, opposite that from which the mouthpiece 4 projects, there is an aperture from which  
10   two walls 11 and 21, respectively (Figure 4), extend outwards from the chamber to converge (Figure 2) towards the exit hole of the nozzle and define a duct for the medicament flow.

It is now unexpectedly found that the aerosol  
15   circulation with a vortex flow into the expansion chamber can be favoured and improved by a particular realization of the nozzle wherein the hole through which the aerosol dose is discharged is inclined (Figure 8).

In accordance with the present invention there is  
20   provided an aerosol nozzle having the shape of a T consisting of an upper horizontal bar and a vertical stem, said stem comprising a socket with a seat for housing a hollow stem of a pressurized can, characterized in that the hole of the vertical stem of the nozzle through which  
25   a dose of medicament discharged from a metering valve finds its way into the expansion chamber is inclined with respect to the hollow stem of the pressurized can.

~~Specific embodiments of the invention will now be~~  
described, with reference to the accompanying drawings, in  
30   which:

Figure 5 is a front view of the T shaped nozzle;

- 5 -

Figure 6 is a side view of the T shaped nozzle;

Figure 7 is a top view of the T shaped nozzle;

Figure 8 is a section view of the nozzle along lines A-A of the Figures 5 and 7, showing the socket provided with a seat to house a hollow stem of a pressurized can and the inclined hole through which a dose of medicament discharged from the valve enters into the expansion chamber.

The nozzle (1) is shaped as a T, consisting of an upper bar composed by two fins (2, 3) to be housed and retained in two seats provided in the two shells forming the device and of a vertical stem (4) shorter than the horizontal upper bar.

The vertical stem (4) comprises a socket (5) provided with a seat to house a hollow stem of a pressurized can.

In the thickness of the stem (4) is bored a hole (6) that connects the socket (5) with the expansion chamber of the device through the orifice (7).

The hole (6) is inclined with respect to the plane B normal to the axis of the vertical stem (4).

When a pressurized can has been housed in the device, with the valve stem inserted into the seat of the socket (5) of the nozzle (1) and the base of the can is pressed with one finger, the dispensing valve within the can opens and a measured quantity of aerosol is discharged.

The discharged aerosol passes through the inclined hole (6) and emerges through the orifice (7) as a cone whose axis is inclined with respect to the plane B.

The axis of the hole and of the emerging aerosol cone forms with the plane B an angle in the range of 20 to 30° and preferably of 27°.

- 6 -

The internal diameter of the hole (6) is in the range of 0.40 to 0.55 mm and is preferably of 0.42 to 0.52 mm.

The inclination of the hole is designed in a manner that the aerosol cone issuing from the nozzle orifice  
5 passes through the duct defined by the two walls 11 and 21 of Figures 3 and 4 extending outwards from the expansion chamber and converging towards the exit hole of the nozzle.

The inclination of the hole is designed in a manner  
10 that the axis of said aerosol cone corresponds with the central plane of the ducts.

It is so avoided any possible deviation of the aerosol jet resulting from the impact of a part of the aerosol cone against the diverging walls 11 and 21.

15 The aerosol cone penetrates into the expansion chamber and generates within the chamber a vortex motion which results in deposition of the largest particles on the walls whereas the other particles lose their layer of propellant and hence reduce in diameter with an increase  
20 of the respirable fraction.

---



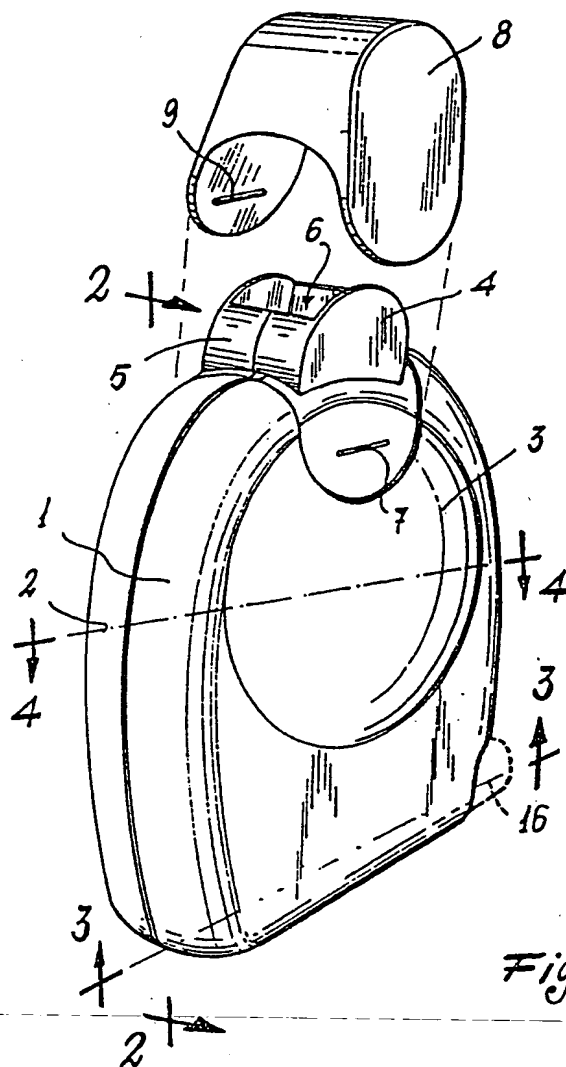
- 7 -

## CLAIMS

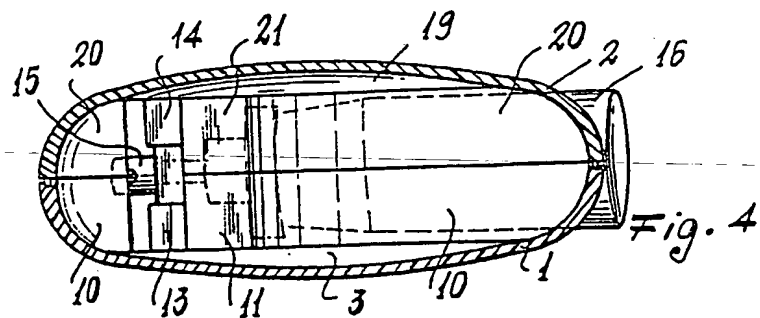
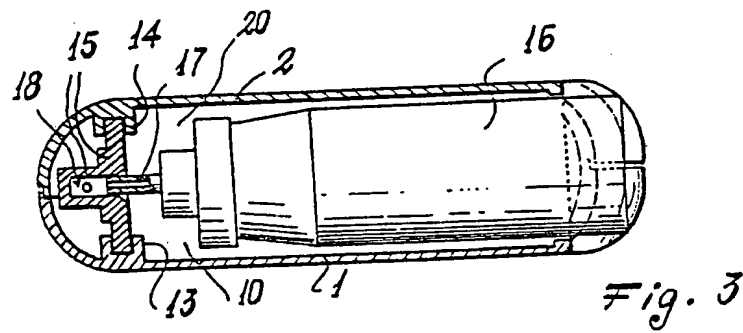
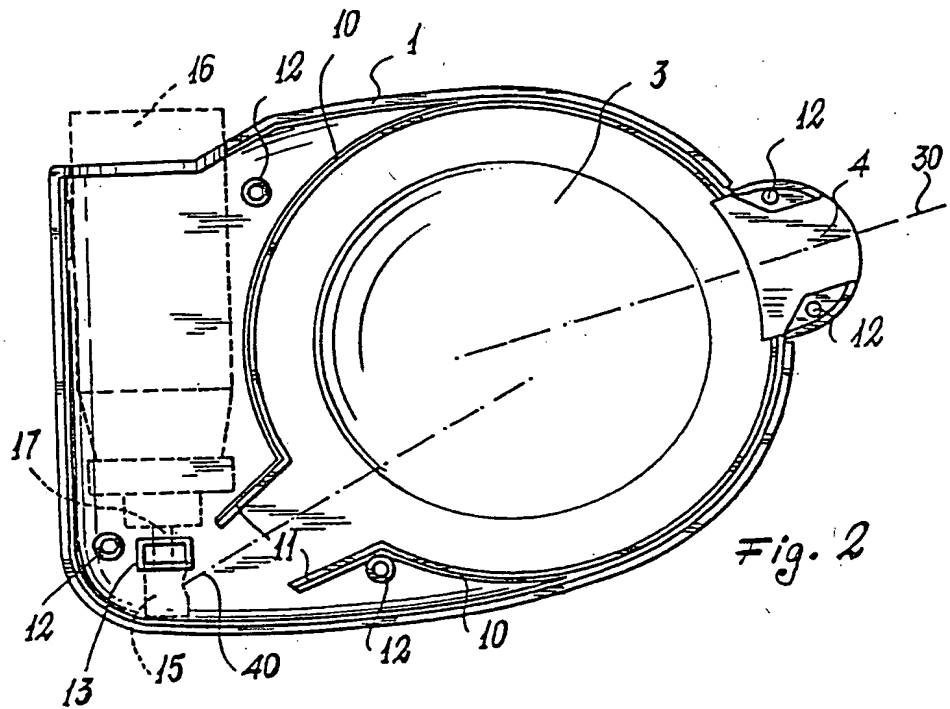
1. An aerosol nozzle, comprising a socket provided with a seat to house a hollow stem of an aerosol dispensing pressurized can, said nozzle being shaped as a T, consisting of an upper bar and of a vertical stem, characterized in that the hole of said nozzle through which the aerosol dose is discharged is inclined with respect to the plane normal to the axis of said vertical stem.
2. A nozzle as claimed in claim 1, characterized in that the axis of the hole and the plane normal to the axis of the stem form an angle in the range of 20 to 30° and preferably of 27°.
3. A nozzle as claimed in claims 1 and 2 wherein the internal diameter of the hole is in the range of 0.40 to 0.55 mm and preferably of 0.42 to 0.52 mm.
4. An aerosol nozzle substantially as herein described, with reference to, and as illustrated in, Fig.5 to 8 of the accompanying drawings.
5. A nozzle as claimed in claims 1 to 4 to be housed in a device for mouth inhaling medicaments dispensed as aerosols by pressurized cans, comprising a body with a seat for housing a can provided with a stem for operating the can dispensing valve, a chamber for the collection and expansion of the aerosol dispensed by a discharged nozzle of the can, and an inhalation mouthpiece communicating with said chamber and projecting outwards from said body, wherein the body is of substantially flat shape, the chamber is delimited by a curved wall, into a first peripheral

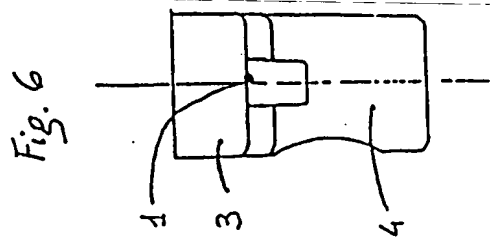
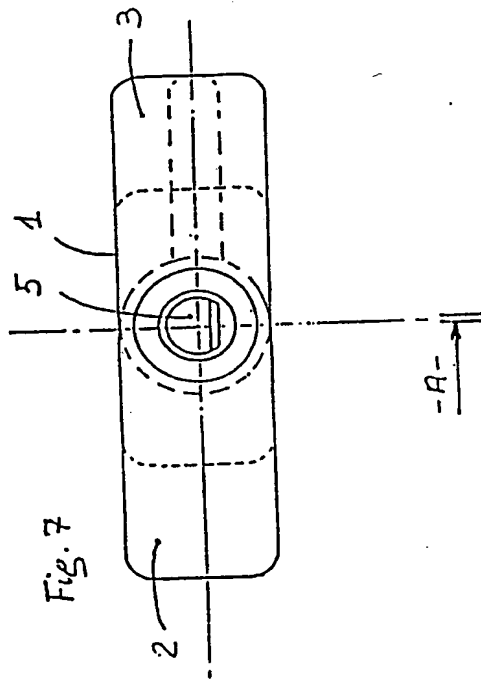
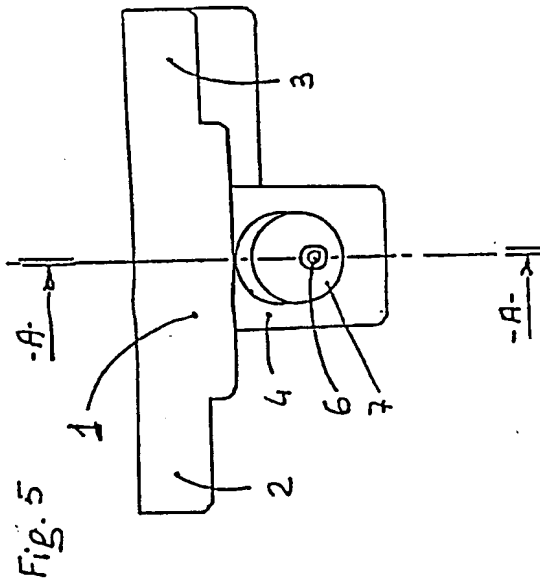
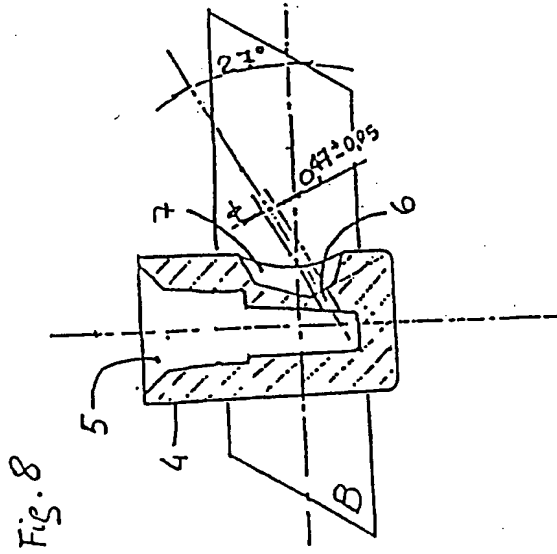
- 8 -

portion of which there opens the inner end of said  
mouthpiece, and in a second peripheral portion of  
which, opposite the first, there is an aperture from  
which two walls extend outwards from the chamber to  
5 converge towards the can discharge nozzle and define  
a duct the centre plane of which is inclined to the  
centre plane of said mouthpiece, characterized in  
that the aerosol discharged by the can circulates  
within the chamber with a vortex flow.



2/3





# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 98/05592

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 6 A61M15/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 475 257 A (CHIESI FARMA SPA) 18 March 1992 cited in the application	1,5
Y	see column 4, line 34 - column 5, line 23; figures	2,3
Y	GB 1 128 655 A (VANTOREX LTD.) 2 October 1968 see page 2, line 85 - line 99; figure 2	2
Y	US 5 622 162 A (RITSON CARL ET AL) 22 April 1997 see column 14, paragraph 4; figures 3-3B	3
A	US 3 517 667 A (BABBIN SAUL A ET AL) 30 June 1970 see claims 1,2; figures	2

-/--

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

5 January 1999

Date of mailing of the international search report

14/01/1999

Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Villeneuve, J-M

## INTERNATIONAL SEARCH REPORT

Internal Application No

PCT/EP 98/05592

**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>GB 2 276 101 A (CSB MOULDS LTD)  21 September 1994</p> <p>-----</p>	

# INTERNATIONAL SEARCH REPORT

Internal Application No  
PCT/EP 98/05592

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0475257 A	18-03-1992	IT 1244441 B AT 107521 T AU 642037 B AU 8373491 A CA 2051172 A DE 69102602 D DE 69102602 T DK 475257 T ES 2061139 T FI 914212 A HU 210440 B IE 65894 B JP 6023048 A NO 300798 B NZ 239626 A PT 98956 A US 5165391 A	15-07-1994 15-07-1994 07-10-1993 19-03-1992 14-03-1992 28-07-1994 06-10-1994 01-08-1994 01-12-1994 14-03-1992 28-04-1995 29-11-1995 01-02-1994 28-07-1997 26-01-1994 30-11-1993 24-11-1992
GB 1128655 A		NONE	
US 5622162 A	22-04-1997	US 5392768 A US 5404871 A US 5755218 A AU 6130394 A WO 9416757 A CA 2082168 C EP 0529053 A JP 9164205 A JP 2613347 B US 5394866 A US 5469750 A US 5450336 A WO 9215353 A US 5522378 A US 5542410 A US 5497764 A US 5520166 A US 5608647 A US 5655516 A US 5743252 A US 5813397 A US 5826570 A	28-02-1995 11-04-1995 26-05-1998 15-08-1994 04-08-1994 26-03-1996 03-03-1993 24-06-1997 28-05-1997 07-03-1995 28-11-1995 12-09-1995 17-09-1992 04-06-1996 06-08-1996 12-03-1996 28-05-1996 04-03-1997 12-08-1997 28-04-1998 29-09-1998 27-10-1998
US 3517667 A	30-06-1970	NONE	
GB 2276101 A	21-09-1994	NONE	